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UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

CELGENE CORPORATION, **Plaintiff,** **v.** **PAR PHARMACEUTICAL, INC., PAR PHARMACEUTICAL COMPANIES, INC., and TEVA PHARMACEUTICALS USA, INC.,** **Defendants.**	**Civil Action No. 17-3159 (ES)(MAH)** **(Filed Electronically)**
CELGENE CORPORATION, **Plaintiff,** **v.** **HETERO LABS LIMITED, HETERO LABS LIMITED UNIT-V, HETERO DRUGS LIMITED, HETERO USA, INC., AUROBINDO PHARMA LIMITED, AUROBINDO PHARMA USA, INC., AUROLIFE PHARMA LLC, EUGIA PHARMA SPECIALTIES LIMITED, APOTEX INC., APOTEX CORP., MYLAN PHARMACEUTICALS, INC., MYLAN INC., MYLAN, N.V., and BRECKENRIDGE PHARMACEUTICAL, INC.,** **Defendants.**	**Civil Action No. 17-3387 (ES)(MAH)** **(Filed Electronically)**

CELGENE'S OPENING *MARKMAN* BRIEF

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Plaintiff Celgene Corporation ("Celgene") submits this brief in support of its proposals for the disputed claim terms of United States Patent Nos. 8,198,262 (the "'262 Patent"), 8,673,939 (the "'939 Patent"), 8,735,428 (the "'428 Patent"), 8,828,427 (the "'427 Patent"), 6,315,720 (the "'720 Patent"), 6,561,977 (the "'977 Patent"), 6,755,784 (the "'784 Patent"), 8,315,886 (the "'886 Patent"), and 8,626,531 (the "'531 Patent") (collectively, the "patents-in-suit") (Ex. 1-9, respectively).[1]

I. INTRODUCTION

The patents-in-suit cover novel aspects of the life-saving drug pomalidomide, all of which were invented by Celgene. Specifically, the patents relate to breakthrough medical uses for pomalidomide, pharmaceutical compositions containing that drug, and methods of safely administering and using the drug.

The parties have identified six disputed claim terms. As discussed herein, some of the disputed terms do not require construction. For those that do, Celgene's constructions derive directly from the intrinsic evidence, are consistent with the extrinsic evidence, and reflect the ordinary meaning of the disputed term. This approach to claim construction follows the Federal Circuit's controlling guidance in *Phillips* and its progeny. By contrast, Defendants' proposed constructions violate several bedrock principles of claim construction. For example, Defendants' proposed constructions would render claim language meaningless in some instances and would read language into the claims in others, despite no support in the intrinsic record for doing so. Accordingly, Celgene respectfully requests that the Court adopt its proposals for the disputed claim terms.

[1] "Ex. __" herein refers to the exhibits to the Declaration of Frank C. Calvosa in support of Celgene's Opening *Markman* brief.

II. BACKGROUND

Celgene is a world-leading biopharmaceutical company that has invented several life-saving cancer therapies. For example, through years of research and development, Celgene invented novel medical uses and formulations of pomalidomide, as well as methods of safely administering and using that drug. Celgene currently sells pomalidomide under the brand name Pomalyst®. The U.S. Food and Drug Administration ("FDA") approved Pomalyst®, in combination with another drug (dexamethasone), to treat patients having a particular type of cancer known as multiple myeloma ("MM")[2] and who have received at least two prior therapies. As a condition of approval, the FDA required the use of Celgene's innovative Pomalyst REMS® to ensure safe administration and use of Pomalyst®. Celgene's inventive methods of treating MM are claimed in the '262, '939, and '428 Patents (the "MM Patents"); Celgene's novel formulations containing pomalidomide are claimed in the '427 Patent (the "Formulation Patent"); and the Pomalyst REMS® is covered by the '720, '977, '784, '886, and '531 Patents (the "REMS Patents").

Defendants are generic pharmaceutical companies that have each filed an Abbreviated New Drug Application ("ANDA") seeking FDA approval to market generic versions of Celgene's Pomalyst® drug product that infringe certain claims of the patents-in-suit. Celgene filed suit against Defendants in May 2017,[3] triggering a statutory stay of FDA approval of

[2] MM is a cancer of certain white blood cells called plasma cells that are normally responsible for producing antibodies. In MM, abnormal plasma cells accumulate in the bone marrow, where they interfere with the production of normal blood cells.

[3] Celgene filed suit against the Hetero, Apotex, Mylan, Aurobindo, and Breckenridge Defendants on May 11, 2017. *See Celgene Corp. v. Hetero Labs Ltd, et al.*, No. 17-3387, D.I. 1 (D.N.J.). Celgene filed suit against the Teva and Par Defendants on May 4, 2017. *See Celgene Corp. v. Par Pharm., Inc., et al.*, No. 17-3159, D.I. 1 (D.N.J.). The Par Defendants have since been dismissed from this action. *See id.* at D.I. 55.

Defendants' ANDAs that remains in effect until August 8, 2020. *See* 21 U.S.C. § 355(j)(5)(F)(ii).

In accordance with the Local Patent Rules, the parties exchanged their proposed claim terms for construction on May 23, 2018, exchanged their preliminary claim constructions and evidence on June 15, 2018, exchanged their Rule 4.2(c) Statements on July 18, 2018, and filed their Joint Claim Construction and Prehearing Statement on August 29, 2018. Therein, the parties identified six disputed claim terms (D.I. 98)[4,5], each of which is discussed below in detail.

III. LEGAL STANDARD

Claim construction is an issue of law. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 970-71 (Fed. Cir. 1995). The Federal Circuit has explained that claim construction starts with the words of the claims. *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1298 (Fed. Cir. 2003). Claim terms are deemed to be read "not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc). In general, the words of a claim are given their plain and ordinary meaning to a person of ordinary skill in the art. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996); *see also 3M Innovative Properties Co. v. Tredegar Corp.*, 725 F.3d 1315, 1321 (Fed. Cir. 2013); *Thorner v. Sony Comput. Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012). "Absent a clear disavowal or contrary definition in the specification or the prosecution history,

[4] All D.I. references herein are to Civil Action No. 17-3159.

[5] The parties originally identified nine disputed claim terms. Since filing the Joint Claim Construction and Prehearing Statement, the parties have agreed that three terms from the '427 Patent ("pregelatinized starch at an amount of [x] mg," "sodium stearyl fumarate at an amount of [x] mg," and "[a]n oral dosage form in the form of a capsule which weighs [x] mg") do not require construction. Those terms are, therefore, no longer in dispute.

the patentee is entitled to the full scope of its claim language." *Home Diagnostics, Inc. v. LifeScan, Inc.*, 381 F.3d 1352, 1358 (Fed. Cir. 2004).

IV. ARGUMENT

For the reasons set forth below, Celgene respectfully requests that the Court adopt its proposals for the disputed claim terms.

A. The MM Patents

The MM Patents claim methods of using pomalidomide to treat MM. Claims 1 and 22 of the '428 Patent are representative; the bolded terms are in dispute:

> 1. **A method of treating multiple myeloma**, which comprises administering to a patient having multiple myeloma, and which patient has received previous therapy for multiple myeloma, from **about 1 mg to about 5 mg per day of a compound having the formula [of pomalidomide] or a pharmaceutically acceptable salt, solvate or stereoisomer thereof** for 21 consecutive days followed by seven consecutive days of rest in a 28 day cycle, wherein the multiple myeloma is relapsed, refractory, or relapsed and refractory multiple myeloma.
>
> 22. **A method of treating multiple myeloma**, which comprises administering to a patient having multiple myeloma, and which patient has received previous therapy for multiple myeloma and has demonstrated disease progression on the previous therapy, from **about 1 mg to about 5 mg per day of a compound having the formula [of pomalidomide] or a solvate thereof**, for 21 consecutive days followed by seven consecutive days of rest in a 28 day cycle.

1. "A method of treating multiple myeloma"

This phrase is the preamble of each independent claim of the MM Patents.[6] The parties dispute whether these method-of-treatment claims require efficacy and, therefore, whether the preamble is limiting.

[6] These claims are: claims 1 and 20 of the '262 Patent, claims 1 and 26 of the '939 Patent, and claims 1 and 22 of the '428 Patent.

Term	Celgene's Proposal	Teva, Mylan, Breckenridge, and Aurobindo's Proposal	Apotex and Hetero's Proposal
"A method of treating multiple myeloma"	"A method of treating multiple myeloma" is limiting, such that the term requires efficacy in treating multiple myeloma	"A method of treating multiple myeloma" is not limiting	"A method of treating multiple myeloma" is not limiting If the term is limiting, then it should be construed as: "A method of administering pomalidomide, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, after the onset of symptoms of multiple myeloma."[7]

Under Celgene's construction, "[a] method of treating multiple myeloma" limits the claims by requiring efficacy in the MM patients receiving pomalidomide. Under Defendants' proposals, the preamble is not limiting and, according to at least the Apotex and Hetero Defendants, by "not limiting," they mean that the claims do not require efficacy. In other words, Defendants argue that Celgene patented giving specific doses of pomalidomide to an MM patient for no reason—a nonsensical proposition.

Celgene's construction—that these ***method-of-treatment*** claims require efficacy—is consistent with the intrinsic record, including the claims, the specification, and the prosecution history. Defendants' construction, on the other hand, is an unsupported, litigation-driven attempt to support Defendants' misguided invalidity theories. Defendants' construction ignores: (1) the intrinsic record, including the clear meaning of the preamble (which requires efficacy), (2) that

[7] Celgene reserves the right to respond to any arguments by any Defendants regarding the meaning of the preamble, including by responding to any related expert testimony offered by Defendants.

the preamble describes a fundamental and essential feature of the invention, and (3) that the Examiner allowed the claims to issue over the prior art because the claimed methods were shown to be efficacious against MM when another therapy had failed. In requiring evidence of efficacy to allow the claims to issue, the Examiner confirmed that efficacy is a required part of the claimed inventions.

(a) The preamble requires efficacy

The intrinsic record makes clear that the preamble requires efficacy against MM—as set forth below, both the specification and prosecution history consistently refer to the invention in terms of efficacy. Ignoring this evidence, Defendants seek to read efficacy—the very crux of the invention—out of the claims. Celgene's construction is supported by the record, and Defendants' litigation-driven proposal lacks merit.

"No litmus test defines when a preamble limits claim scope." *Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002). "Whether a preamble stating the purpose and context of the invention constitutes a limitation of the claimed process is determined on the facts of each case in light of the overall form of the claim, and the invention as described in the specification and illuminated in the prosecution history." *Id.* (citation omitted). In *Catalina*, the Federal Circuit recognized that "[s]ome guideposts . . . have emerged from various cases discussing the preamble's effect on claim scope." *Id.* In particular, the court noted that a preamble is limiting where it: (1) "recites essential structure or steps"; (2) provides antecedent basis for terms in the body of the claim; (3) is repeated in the specification; or (4) was "clearly" relied upon during the prosecution to distinguish the claimed invention from prior art. *Id.* at 808-09; *see also Helsinn Healthcare S.A. v. Dr. Reddy's Labs., Ltd.*, No. 11-3962, 2015 WL 1817109, at *2-3 (D.N.J. Apr. 22, 2015).

Before engaging in this analysis, it is necessary to understand the meaning of the preamble in this case—as the *Catalina* Court put it, "in light of the overall form of the claim, and the invention as described in the specification and illuminated in the prosecution history." 289 F.3d at 808.[8] The Federal Circuit has "held that the purpose of the invention may guide claim construction since 'the problem the inventor was attempting to solve, as discerned from the specification and prosecution history, is a relevant consideration' in construing claims." *NEC Corp. v. Hyundai Elecs. Indus. Co.*, 30 F. Supp. 2d 546, 553 (E.D. Va. 1998) (quoting *CVI/Beta Ventures, Inc. v. Tura LP*, 112 F.3d 1146, 1160 (Fed. Cir. 1997)). "Claim construction must account for the [stated] purpose of the patented invention." *Cobalt Boats, LLC v. Brunswick Corp.*, No. 15-21, 2017 WL 6034504, at *5 n.2 (E.D. Va. Dec. 4, 2017) (citing *Innovad Inc. v. Microsoft Corp.*, 260 F.3d 1326, 1332-33 (Fed. Cir. 2001)). As such, a court must "construe the claim in a way that does not negate its major purpose." *Neev v. Alcon Labs., Inc.*, No. 15-00336, 2016 WL 9051170, at *3 (C.D. Cal. Dec. 22, 2016). Here, "[a] method of treating multiple myeloma" requires efficacy against MM. If not, then the invention would lose its entire purpose. That is neither what the inventors intended, nor what the intrinsic evidence shows.

Rather, the specification stresses that "there is a significant need for safe and ***effective*** methods of treating, preventing and managing cancer and other diseases and conditions, particularly for diseases that are refractory to standard treatments . . . ." (Ex. 1 at 3:8-11 (emphasis added).)[9] In other words, the entire framework of the invention, and the existing need that it seeks to address, requires efficacy.

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[8] Notably, four of the six Defendants do not provide a proposed construction for the "method of treatment multiple myeloma" portion of the claimed inventions. Instead, they seek to erase that language from the inventions.

[9] The MM Patents share a common specification. For convenience, citations to the specification are listed only for the '262 Patent. Both Celgene and Defendants agree that there are

The specification goes on to explain that "[a] number of studies have been conducted with the aim of providing compounds that can safely and ***effectively*** be used to treat diseases . . . ." (*Id.* at 3:16-17 (emphasis added).) The "Summary of the Invention" further drives this point home:

> This invention encompasses methods of treating and preventing certain types of cancer, including primary and metastatic cancer, as well as cancers that are refractory or resistant to conventional chemotherapy. The methods comprise administering to a patient in need of such treatment or prevention a ***therapeutically or prophylactically effective*** amount of an immunomodulatory compound, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof.

(*Id.* at 3:41-47 (emphasis added); *see also, e.g.*, *id.* at 3:63-4:3 (same); *id.* at 4:34-40 (same).) In the case of the claimed inventions, that effective amount includes 1 to 5 mg of the immunomodulatory compound pomalidomide. (*See, e.g.*, *id.* at claims 1, 10-13, 18, 20-24 and 26; 18:15-19, 18:24-27, 22:51-57, 24:28-35, 26:60-63, 33:20-23.)

The specification also discusses combining the immunomodulatory compounds of the invention (including pomalidomide) with "Second Active Agents" (including dexamethasone), and notes that "certain combinations work synergistically in the treatment of particular types of cancer . . . ." (*Id.* at 11:47-52.) In other words, the patent focuses on methods of treatment using "***active***" ingredients that "***work synergistically***." The specification describes these combinations as follows:

> The combined use of the immunomodulatory compounds of the invention and conventional therapy may provide a unique treatment regimen that is ***unexpectedly effective*** in certain patients. Without being limited by theory, it is believed that immunomodulatory compounds of the invention may provide

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"corresponding citations" in the specifications of the '939 and the '428 Patents, and Celgene relies on those corresponding citations here. *See* D.I. 98, Ex. A at 2 n.5, n.7.

> ***additive or synergistic effects*** when given concurrently with conventional therapy.

(*Id*. at 22:35-41 (emphasis added).)

The specification also discusses the claimed dosing cycles in the context of efficacy. In particular, the specification notes that cycling therapy (such as that claimed in the MM Patents) can be used to, among other things, "improve[] the ***efficacy*** of the treatment." (*Id.* at 24:5-13 (emphasis added); *see also id.* at 32:50-53.)

The Examples that discuss "Clinical Studies in Patients" also discuss the claimed methods in terms of efficacy. For example, Example 6.5.1, which discusses a clinical trial with pomalidomide, refers to the "Southwest Oncology Group (SWOG) criteria," which is a standard means of assessing MM disease status and progression that relies on measuring the presence of monoclonal plasma protein ("M-Protein") in human blood. (*See, e.g.*, *id.* at 33:11-17; *see also id.* at 35:24-29 ("Response to treatment was assessed by M-Protein quantification . . . .").)

The prosecution history also makes clear that the claimed methods require efficacy. For example, as explained in more detail below, during prosecution of the MM Patents, the applicants relied on the efficacy of the claimed methods to overcome the Examiner's rejections under 35 U.S.C. § 103. *See infra* at § IV.A.1.(b).(ii).

In sum, the intrinsic record makes clear that the claimed methods, through the preamble, require efficacy. The Court should therefore adopt Celgene's proposal for "[a] method of treating multiple myeloma." Adopting Defendants' position that the preamble is not limiting, and therefore does not require efficacy, would negate the purpose of the claimed inventions.

(b) The preamble is limiting

(i) The efficacy required by the preamble is a fundamental or essential feature of the invention

Defendants' contention that the preamble of the MM Patents should not be considered a claim limitation lacks merit. Following the first guidepost in *Catalina*, this District has found preambles limiting where they describe an essential or "fundamental" feature of the invention. For example, in *AstraZeneca Pharm. LP v. Handa Pharm.*, Judge Pisano found the preamble "[a] sustained release formulation" to be limiting because the "[t]he entire specification of the '437 Patent and all examples are directed to sustained release formulations." No. 08-3773, 2010 WL 4941431, at *3 (D.N.J. Nov. 30, 2010). Judge Pisano explained that the "sustained release aspect of the formulations is a fundamental feature of the claimed invention, and thus is an element of the claims." *Id.*; *see also Vizio, Inc. v. Int'l Trade Comm'n*, 605 F.3d 1330, 1340 (Fed. Cir. 2010) (holding that a preamble is limiting where it sets forth "the essence or a fundamental characteristic of the claimed invention.") Similarly, in *Manning v. Paradis*, the Federal Circuit held that a preamble reciting "a method of treating a subject in cardiac arrest" with oxygen was limiting, stating that "the preamble defines the intended purpose of the invention because unless oxygen were delivered to the heart of the subject in a ***therapeutic*** amount the invention would have no purpose." 296 F.3d 1098, 1099, 1103 (Fed. Cir. 2002) (emphasis added).

Likewise, here, ***efficacy*** against MM is a fundamental feature of the invention. As in *AstraZeneca* and as described above in detail, the intrinsic record makes clear that the recited methods of treatment require efficacy. *See supra* at § IV.A.1.(a). Given that the efficacy limitation is set forth only in the preamble, and not elsewhere in the claim, the preamble must be considered a claim limitation. *See, e.g.*, *Tanita Corp. v. Homedics-U.S.A., Inc.*, No. 08-7145,

2010 WL 4625228, at *7 (N.D. Ill. Nov. 4, 2010) (finding preamble limiting where recited feature was "not disclosed in the body of the asserted claims . . . is repeatedly referenced throughout the specification . . . [and] recites essential language which, if deleted, would 'affect the structure . . . of the claimed invention.'") Without a limiting preamble, the "invention would have no purpose." *Manning*, 296 F.3d at 1103.

In light of the foregoing, it is clear that the preamble—including efficacy—is a fundamental or essential feature of the claimed inventions. As such, the Court should find that the preamble is a claim limitation, and reject Defendants' attempt to render the invention meaningless.

(ii) Patentability of the claimed methods depends upon efficacy

As an independent basis for finding that the preamble is limiting, it is axiomatic that where claim language is "material to patentability," it is limiting. *See Allergan Sales LLC v. Sandoz, Inc.*, No. 17-10129, 2018 WL 3675235, at *5 (D.N.J. July 13, 2018) (collecting cases and holding "that claim terms stating the unexpected and improved effects of the administration of a claimed compound may be limiting if they express the invention"). Focusing on the fourth *Catalina* "guidepost," the Federal Circuit has held that it "must" give preambles "weight, [where] the patentability of the claims hinged upon their presence in the claim language." *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1330, 1333 (Fed. Cir. 2003) (finding the preamble "[a] method of treating or preventing anemia in humans" to be limiting).

Likewise, here, the preamble—"[a] method of treating multiple myeloma"—is limiting because it is the basis upon which the Patent Office allowed the claims. The Examiner allowed each of the MM patents to issue specifically because the inventions claimed therein demonstrated ***efficacy*** against MM. For example, during prosecution of both the '939 and '428

Patents, the claims issued only ***after*** Celgene submitted evidence of "unexpected ***results***," namely "that one skilled in the art would not have expected that pomalidomide would be able to ***treat*** multiple myeloma that is relapsed after or refractory to prior treatment." (*See* Ex. 10 at CELPOM00001074 (emphasis added); Ex. 11 at CELPOM00001375 (emphasis added).) Thus, when the inventors referred to "treat[ing] multiple myeloma" in the prosecution history, they meant that pomalidomide was providing efficacy against MM. That was the Examiner's understanding as well.

In fact, the Examiner explained in an Interview Summary immediately preceding the Notice of Allowance that the claims would issue because the invention "was shown to unexpectedly ***treat*** multiple myeloma that is or has become resistant to lenalidomide (LEN), a structurally close analog of [pomalidomide] that is known to be ***effective for treating multiple myeloma***." (*See* Ex. 12 at CELPOM00001113 (emphasis added); Ex. 13 at CELPOM00001414 (emphasis added).) In other words, the claims issued only because the inventors demonstrated to the Examiner that their invention was efficacious against MM. The file history cannot be read to mean that pomalidomide was simply given to the MM patients with no results. Rather, the evidence specifically refers to the ***results***: patients' responses to pomalidomide. As in *Jansen*, the preambles of the MM Patents must be given weight because "the patentability of the claims hinged upon their presence in the claim language." 342 F.3d at 1333.

Because the prosecution history makes clear that the claims would not have issued absent evidence that the claimed methods resulted in ***efficacy*** against MM, which is conveyed through the preamble, the Court should construe "a method of treating multiple myeloma" as a claim limitation.

2. "about 1 mg to about 5 mg per day of a compound having the formula [of pomalidomide] or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof";[10]

"about 1 mg to about 5 mg per day of a compound having the formula [of pomalidomide] or a solvate thereof"[11]

These limitations reflect the fact that the claimed methods include treating the MM patient with pomalidomide in several pharmaceutically acceptable forms, including as a free base, salt, solvate, or stereoisomer. Celgene's proposed constructions reflect the plain and ordinary English meaning of the words used in the claims. Defendants' proposals are tortured reconstructions of plain language that are not supported by the intrinsic record.

Term	Celgene's Proposal	Defendants' Proposal
"about 1 mg to about 5 mg per day of a compound having the formula [of pomalidomide] or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof"	"about 1 mg to about 5 mg per day of a compound having the formula [of pomalidomide] or a pharmaceutically acceptable salt, solvate, or stereoisomer containing about 1 mg to about 5 mg per day of a compound having the formula [of pomalidomide]"	"about 1 mg to 5 mg ... of a compound having the formula [of pomalidomide] or about 1 mg to 5 mg of a pharmaceutically acceptable salt or solvate of [pomalidomide] or about 1 mg to 5 mg of any single stereoisomer of [pomalidomide]"
"about 1 mg to about 5 mg per day of a compound having the formula [of pomalidomide] or a solvate thereof"	"about 1 mg to about 5 mg per day of a compound having the formula [of pomalidomide] or a solvate containing about 1 mg to about 5 mg per day of a compound having the formula [of pomalidomide]"	"about 1 mg to 5 mg ... of a compound having the formula [of pomalidomide] or about 1 mg to 5 mg of a solvate of [pomalidomide]"

It is well understood that a salt or solvate of an active pharmaceutical ingredient ("API") weighs more than that same ingredient in a non-salt or non-solvated form. The reason for this is simple: to create a salt or solvate of a drug, such as pomalidomide, other molecules must be

[10] This phrase appears in claim 1 of each MM Patent.

[11] This phrase appears in claim 26 of the '939 patent and claim 22 of the '428 Patent.

added to it. (*See, e.g.*, Ex. 1 at 9:57-10:13 (explaining that "'pharmaceutically acceptable salt' encompasses non-toxic acid and base addition . . . ").) Stereoisomers, on the other hand, are molecules with the same molecular formula (and, therefore, same weight), but with different three-dimensional structures.[12]

Here, the claims require a certain amount of pomalidomide—"about 1 mg to about 5 mg per day of [pomalidomide]"—or a salt, solvate, or stereoisomer that includes that ***same amount*** of pomalidomide. Per the claim language, a salt of pomalidomide would contain about 1 mg to about 5 mg of pomalidomide, but the salt of pomalidomide would ultimately weigh more than that because of the addition of the molecules forming the salt. The claims also include the word "thereof," which refers back to the specifically claimed amounts of pomalidomide. Accordingly, the "about 1 to about 5 mg" modifies the amount of pomalidomide, and does not separately modify the amount of the salt, solvate, or stereoisomer of pomalidomide. In other words, the claims call for treatment with about 1 to about 5 mg of pomalidomide itself, regardless of whether the pomalidomide is in the form of a salt, solvate, or stereoisomer.

Defendants' proposals are litigation-driven efforts to create confusion where none exists, and which fail to find any support in the intrinsic record. In light of the foregoing, the "about 1 mg to about 5 mg" terms should be construed as Celgene proposes: in accordance with their plain and ordinary language.

[12] Stated differently, isomers contain the same number of atoms of each element, but have different arrangements of those atoms in space.

B. The Formulation Patent

The '427 Patent claims pharmaceutical formulations containing pomalidomide. Claim 3 of the '427 Patent is representative, with the disputed term shown in bold:

> 3. An oral dosage form in the form of a capsule which weighs 125 mg and comprises: 1) pomalidomide, or a pharmaceutically acceptable salt or solvate thereof, at an amount that provides 1 mg of 100% pure pomalidomide; 2) pregelatinized starch at an amount of 70 mg; 3) sodium stearyl fumarate at an amount of 0.32 mg; and 4) spray dried mannitol at an amount that brings **the total weight of the composition** to 125 mg.[13]

Defendants Apotex and Hetero ***agree*** with Celgene that no construction is necessary for this term. The Teva, Mylan, Breckenridge, and Aurobindo Defendants, however, seek to read limitations into the claims that neither reflect the claims' plain meaning nor are supported by the intrinsic record. The Teva, Mylan, Breckenridge, and Aurobindo Defendants also improperly propose a construction that obscures the meaning of an otherwise ordinary phrase. Specifically, these Defendants assert that "total weight of the composition" should be construed to mean "total weight of the composition ***including the weights of counter ions and solvent molecules, if present***," without offering any proposed meaning for the additional words they seek to insert into the easily-understood claim language.

Term	Celgene's Proposal	Teva, Mylan, Breckenridge, and Aurobindo's Proposal	Apotex and Hetero's Proposal
"total weight of the composition"	No construction necessary.	"total weight of the composition including the weights of counter ions and solvent molecules, if present"	No construction necessary.

[13] This phrase appears in claims 3, 5, 7, and 9 of the '427 Patent.

This Court and others routinely find that "no construction necessary" is a proper approach to claim construction where claim terms have a well-understood meaning. *See, e.g.*, *Supernus Pharm. Inc. v. Actavis Inc.*, No. 13-4740, 2016 WL 527838, at *5 (D.N.J. Feb. 5, 2016); *Schindler Elevator Corp. v. Otis Elevator Co.*, No. 09-0560, 2010 WL 199600, at *6 (D.N.J. Jan. 13, 2010) (finding no construction necessary where "the ordinary meaning of claim language as understood by a person of skill in the art [is] readily apparent"); *Mobile Telecommnc's Techs., LLC v. United Parcel Service, Inc.*, No. 12-3222, 2014 WL 1274003, *6-7 (N.D. Ga. Mar. 17, 2014) ("It is true that in some circumstances, the Court may properly decline to construe a term if it is clear that [the factfinder] would understand the term without further construction"); *Comcast Cable Commc'ns. v. Sprint Commc'ns*, 38 F. Supp. 3d 589, 604 (E.D. Pa. 2014) ("because [Defendant's] construction provides no additional insight into the meaning to either term, the Court concludes that further construction is unnecessary").

Here, the intrinsic record does not support the proposal offered by Teva, Mylan, Breckenridge, and Aurobindo. Teva, Mylan, Breckenridge, and Aurobindo simply repeat the phrase that they contend requires construction, then add "including the weights of counter ions and solvent molecules, if present." These Defendants do not explain why they have randomly selected only "counter ions" and "solvent molecules" to include within the total weights. They also ignore that the phrase "total weight of the composition" appears repeatedly throughout the specification, yet not once does it refer to some undefined "counter ions" or "solvent molecules." (*See, e.g.*, '427 Patent (Ex. 4) at 5:62-6:27; 6:34-67; 7:11-25; 7:44-8:2.) Defendants' attempt to read these additional elements into the claims is improper. *See McCarty*, 160 U.S. at 116 ("[W]e know of no principle of law which would authorize us to read into a claim an element which is not present."); *ActiveVideo*, 694 F.3d at 1326 (affirming district court's conclusion that claims

did not require construction where the "proposed construction erroneously reads limitations into the claims").

Furthermore, these Defendants do not explain what their additional words supposedly mean. Adopting their construction would only lead to a future dispute that would require the Court to discern the meaning of these added words, without any guidance from the intrinsic record. Defendants' approach should be rejected for this additional reason. *See Depomed, Inc. v. Sun Pharma Glob. FZE*, No. 11-3553, 2012 WL 3201962, at *5 (D.N.J. Aug. 3, 2012) (citation omitted) (rejecting "Defendants' proposed construction [that] would itself require additional defining," noting, that "the words the court uses in construing a claim should not be limitations that require additional interpretation."). Accordingly, the Court should find that this term does not require construction.

C. The REMS Patents

The REMS Patents cover inventive methods of safely administering and using Celgene's Pomalyst® product. In particular, the REMS Patents cover Celgene's novel methods of safely administering and using potentially teratogenic drugs—including Pomalyst®—through the FDA-approved and mandated Pomalyst REMS® (or Risk Evaluation and Mitigation Strategy).

Celgene's first inventive methods of safely administering and using such drugs were first patented in U.S. Patent No. 6,045,501 (the "'501 Patent"). Celgene subsequently improved upon the inventions described in the '501 Patent by, among other things, requiring an independent risk assessment before a pharmacist is allowed to dispense a drug, regardless of what the doctor may have prescribed. This improvement allows for prospective interventions and serves as a secondary check to prevent situations where, for example, a doctor improperly prescribes a drug.

The parties have identified four disputed terms in the REMS Patents, all of which relate to the claimed improvements: "prescription approval code," "computer readable storage

medium," "computer readable medium," and "a generator configured to generate a prescription approval code." Celgene's proposed constructions are supported by both the intrinsic record and extrinsic evidence and reflect the plain and ordinary meaning of the disputed terms. Defendants' proposals contradict the patent specification and/or prosecution history, and thus run afoul of *Phillips*.

1. "Prescription approval code"[14]

Term	Celgene's Proposal	Defendants' Proposal
"prescription approval code"	"a code representing that an affirmative risk assessment has been made based upon risk-group assignment and the information collected from the patient, and that is generated only upon a determination that the risk of a side effect occurring is acceptable"	"code representing consent to fill a prescription"

(a) Celgene's proposal is supported by intrinsic and extrinsic evidence

Celgene's proposed construction of "prescription approval code" is ***the same construction adopted by the Patent Trial and Appeal Board*** ("PTAB") during *inter partes* review ("IPR") of one of the REMS Patents. *See Coalition for Affordable Drugs VI, LLC v. Celgene Corp.*, IPR2015-01096[15], Paper 73 at 15 (PTAB Oct. 26, 2016) (Ex. 14). That is because Celgene's proposed construction is supported by both the intrinsic and extrinsic

[14] This phrase appears in claim 1 of the '720 Patent, claims 1 and 7 of the '977 Patent, claims 1 and 7 of the '784 Patent, claims 1, 5, and 7 of the '886 Patent, and claims 1, 4, 13, 21, 24, 33, and 38 of the '531 Patent.

[15] For convenience, only references to IPR2015-01096 are provided, but the Final Written Decisions for two other IPRs contained the same claim construction analysis.

evidence, including the understanding of this term to persons of ordinary skill in the art (as evidenced by the PTAB's decision).[16]

Intrinsic evidence is "the most significant source of the legally operative meaning of disputed claim language." *Vitronics Corp*, 90 F.3d at 1582. "[A]rguments made during prosecution regarding the meaning of a claim term are relevant to the interpretation of that term in every claim of the patent absent a clear indication to the contrary." *Southwall Techs. Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1579 (Fed. Cir. 1995). In other words, "[t]he prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution." *Id.* at 1576-77; *see also Sunovion Pharm. v. Teva Pharm. USA, Inc.*, 731 F.3d 1271, 1276 (Fed. Cir. 2013) (affirming construction of term consistent with how patentee used it during prosecution).

The file history for the REMS Patents mandates Celgene's proposed construction. During prosecution of the '720 Patent, the examiner alleged that a reference (Boyer) disclosed the same prescription approval code as recited in the '720 Patent's claims. (Ex. 15 at CELPOM10000139-140). The applicants, however, successfully overcame that rejection and distinguished Boyer as follows:

> Claim 1 further requires an assessment, based upon the risk group assignment and the information collected from the patient, as to whether the risk of the side effect occurring is acceptable. Upon a determination that the risk is acceptable, *and only upon such a determination*, a prescription approval code is generated, which must be retrieved by the pharmacy before the prescription may be filled. Thus, the prescription approval code is not merely a number that is associated with the prescription, but instead represents the

[16] During the IPRs, the PTAB upheld Claim 10 of the '720 Patent as patentable, but found Claims 1-9 and 11-32 of the '720 Patent unpatentable. The PTAB's decisions regarding the '720 Patent are currently on appeal at the Federal Circuit, and claims 1-9 and 11-32 remain valid and enforceable during the pending appeal. No claims of any other REMS Patents were challenged in IPRs and, therefore, each of those claims remains valid and enforceable.

> fact that a determination has been made that the risk of the side effect occurring is acceptable, and that approval – an affirmative decision – has been made for the prescription to be filled.

(Ex. 16 at CELPOM10000146-147 (emphasis original).)

The applicants further clarified that, unlike the '720 Patent's claims, "Boyer does not disclose or suggest such an approval code." (*Id.* at CELPOM10000147.) In fact, the applicants noted that the code in Boyer "is simply an identifier for the prescription, and is not an *approval code*, as recited in Applicants' claims." (*Id.* (emphasis original).) The prosecution history shows that the inventors intended for the prescription approval code to require an ***affirmative decision*** based upon review of the patient's risk-group assignment and other collected information, and that is generated only upon a determination that the risk of a side effect occurring is acceptable. Thus, the prosecution history supports Celgene's proposal. *See, e.g.*, *Phillips*, 415 F.3d at 1317 ("[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution . . . .").

The PTAB agreed with Celgene's reading of the prosecution history. *See Coalition for Affordable Drugs VI*, IPR2015-01096, Paper 73 at 15. The PTAB also recognized that extrinsic evidence supported Celgene's proposed construction. Specifically, the ***opposing expert*** "agreed that the claimed prescription approval code represented a determination that the risk of a side effect occurring was acceptable and that approval and affirmative decision had been made for the prescription to be filled." *See id.* (emphasis original). Thus, the understanding of this term to a person of ordinary skill in the art also supports Celgene's proposed construction.

Celgene's proposed construction is the correct one; the PTAB recognized this, and the Court should as well.

(b) Defendants' proposal seeks to trivialize the disputed term and is contrary to the evidence

Defendants' proposal—that the term "prescription approval code" should be construed as a "code representing consent to fill a prescription"—ignores the intrinsic and extrinsic evidence and instead reflects a litigation-inspired attempt to read the invention out of the claims in a transparent effort to bolster Defendants' misguided invalidity theories. Simply put, it deviates from *Phillips* and should be rejected.

Moreover, as Celgene argued during prosecution, "[t]he prescription approval code is not merely a number that is associated with the prescription, but instead represents the fact that a determination has been made that the risk of the side effect occurring is acceptable. . . ." (Ex. 16 at CELPOM10000147.) Defendants ignore this and propose a construction that is essentially "a number that is associated with a prescription," rather than the multi-step, affirmative risk assessment that was explained during prosecution. Defendants' proposal is an attempt to trivialize an otherwise unambiguously defined term.

2. "Computer readable storage medium" and "computer readable medium"[17]

Term	Celgene's Proposal	Defendants' Proposal
"Computer readable storage medium"	"a centralized database that includes all registration information regarding the claimed prescribers, pharmacies, and patients"	No construction necessary, but if construed, should be construed to have its plain and ordinary meaning, which is "computer readable storage medium, which may or may not be centralized"

[17] These phrases appear in claims 1, 5, 6, and 28 of the '720 Patent, claims 1 and 7 of the '977 Patent, claims 1 and 7 of the '784 Patent, claims 1 and 5 of the '886 Patent, and claims 1, 2, 12, 17, 20, 21, and 40 of the '531 Patent.

"computer readable medium"	"a centralized database that includes all registration information regarding the claimed prescribers, pharmacies, and patients"	No construction necessary, but if construed, should be construed to have its plain and ordinary meaning, which is "computer readable storage medium, which may or may not be centralized"

(a) The intrinsic and extrinsic evidence supports Celgene's proposed construction

The specification consistently refers to the "computer readable storage medium[18]" as a database that, among other things, maintains registration information for pharmacies, prescribers, and patients. Moreover, the claim language and prosecution history indicate that the medium must be centralized.

"Words of a claim are generally given their ordinary and customary meaning, which is the meaning a term would have to a person of ordinary skill in the art after reviewing the intrinsic record at the time of the invention." *O2 Micro Int'l Ltd. v. Beyond Innovation Tech. Co.*, 521 F.3d 1351, 1360 (Fed. Cir. 2008). Throughout the specification, Celgene unambiguously and repeatedly refers to the "computer readable storage medium" as the repository for the registration information for pharmacies, prescribers, and patients. For example, the specification states that "prescriptions for the drug are filled only after a computer readable storage medium has been consulted to assure that the prescriber is registered in the medium and qualified to prescribe the drug, that the pharmacy is registered in the medium and qualified to fill the prescription for the drug, and the patient is registered in the medium and approved to receive the drug." (Ex. 5 at 2:54-60; *see also id.* at 4:43-6:10; 8:27-38; 13:18-32; and 18:20-26.) Thus, the specification expressly links the term "computer readable storage

[18] For convenience, Celgene treats these two terms together, and all the references to "computer readable storage medium" apply equally to "computer readable medium."

medium" with the registration information for prescribers, pharmacies, and patients. Celgene's proposed construction reflects that disclosure. Defendants, however, omit any reference to this association.

Moreover, although the specification discloses that the above-described information may be stored in "one or more appropriate computer readable storage media" (Ex. 5 at 8:30-33), ***the language of the claims*** limits the specific inventions set forth in the REMS Patents to a ***centralized*** computer readable medium. First, the term "computer readable storage medium" is used in representative claim 1 of the '720 Patent as follows: (1) consulting "a computer readable storage medium" to obtain a prescription approval code; (2) registering prescribers in "said medium;" (3) registering pharmacies in "said medium;" (4) registering patients in "said medium;" and (5) entering risk group assignments into "said medium." (Ex. 5 at 18:20-36.) "Subsequent use of the definite articles 'the' or 'said' in a claim refers back to the ***same*** term recited earlier in the claim." *Wi-Lan, Inc. v. Apple, Inc.*, 811 F.3d 455, 462 (Fed. Cir. 2016) (emphasis added). Applied to the claims here, use of the article "a," followed by four instances of "said," indicates that these four references are referring back to the ***same*** computer readable storage medium described earlier. Thus, there is only ***one centralized computer readable storage medium***, and it contains the registration information for prescribers, pharmacies, and patients. This is consistent with Celgene's proposed construction.

In addition, extrinsic evidence also supports Celgene's proposal. During prosecution of the '501 Patent (the patent upon which the '720 Patent's Jepson claims[19] are based), the applicants overcame a prior-art rejection by defining "computer readable storage medium" as a

[19] Jepson claims are drafted as a general description of the known elements of the claimed invention (here, those elements were previously claimed in the '501 patent), and the novel improved elements set forth after the "improvement comprising" clause. *See* 37 C.F.R. § 1.75(e) (describing the preferred format for claims to improvements).

centralized storage medium. There, the Examiner alleged that a reference disclosed registering prescribers, pharmacies, and patients in a computer readable storage medium. (Ex. 17 at 2.) The applicants distinguished the art on the grounds that the claimed storage medium, unlike that in the prior art, was ***centralized***:

> Sloane fails also to teach methods in which the information regarding the parties involved in the disclosed methods, for example physician, pharmacy and patient, are registered in a ***central*** computer readable storage medium.

(Ex. 18 at 5 (emphasis added).) Further, the applicants distinguished the claims of the '501 Patent from the reference on the grounds that the claims "define[d] methods for ***centralizing*** certain information in a computer readable medium." (*Id.* (emphasis added).) Because the '720 Patent presents Jepson claims that are directed towards improvements to the inventions set forth in the '501 Patent (*see, e.g.*, Ex. 5 at 1:65-2:12), the "computer readable storage medium" of the '720 Patent (and, thus, all REMS Patents) is the same computer readable storage medium set forth in the '501 Patent. The inventors intended for it to carry the same meaning.

Accordingly, the intrinsic and extrinsic evidence show that the prescriber, pharmacy, and patient must be registered in a ***centralized*** computer readable storage medium.

(b) Defendants' proposal ignores the evidence

Defendants contend that the term "computer readable storage medium" requires no construction, but if construed, it should be afforded an alleged plain and ordinary meaning of "computer readable storage medium, which may or may not be centralized."

Defendants, however, merely repeat the words of the claim, and ignore the evidence discussed above that supports a requirement that the storage medium is a centralized storage medium. Defendants' proposal should be rejected.

3. "A generator configured to generate a prescription approval code"[20]

Term	Celgene's Proposal	Defendants' Proposal
"A generator configured to generate a prescription approval code"	"prescription approval code" means "a code representing that an affirmative risk assessment has been made based upon risk-group assignment and the information collected from the patient, and that is generated only upon a determination that the risk of a side effect occurring is acceptable" No construction necessary for remainder of proposed language	Indefinite

Celgene has already addressed the construction of the term "prescription approval code" above, and expressly incorporates that discussion here. Regarding the remainder of the term, no additional construction is necessary. Celgene reserves the right to respond to any of Defendants' arguments regarding indefiniteness in their responsive *Markman* papers.

To the extent that Defendants intend to argue that this term renders the claims in which it appears indefinite because it is allegedly a means-plus-function term governed by 35 U.S.C. § 112 ¶ 6, Defendants are mistaken. The Federal Circuit has long held that use of the word "means" creates a presumption that § 112, ¶ 6 applies. *Williamson v. Citrix Online, LLC*, 792 F.3d 1339, 1349 (Fed. Cir. 2015). Conversely, lack of the term "means" creates the opposite presumption: that the claim is ***not*** a means-plus-function claim, and that § 112 ¶ 6 does ***not*** apply. *Id.*; *Power Integrations, Inc. v. Fairchild Semiconductor Int'l, Inc.*, 711 F.3d 1348, 1364 (Fed. Cir. 2013) (citing *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1369 (Fed. Cir.

[20] This phrase appears in claim 1 of the '531 Patent.

2002) ("If a claim does not use the word 'means,' we presume that means-plus-function claiming does not apply."). The claims of the '531 Patent do ***not*** use the word "means," thus invoking the presumption ***against*** the applicability of 35 U.S.C. § 112, ¶ 6. Defendants have not rebutted this presumption, and they cannot do so. Thus, the presumption stands, and this is not a means-plus-function term. Accordingly, Defendants' apparent indefiniteness argument fails.

V. CONCLUSION

For the foregoing reasons, Celgene respectfully requests that the Court reject Defendants' proposed constructions and adopt Celgene's proposals for each disputed term and phrase.

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